

WHAT IS CLAIMED IS

1. Resorbable bone substitute for *in vivo* implantation, comprising bone cement material, an antimicrobial agent and a bone growth factor, wherein

- 5 - the antimicrobial agent has a fast release profile, and
 - the bone growth factor has a slow release profile.

2. Resorbable bone substitute according to claim 1, wherein the growth factor is uncharged at physiological pH.

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3. Resorbable bone substitute according to claim 1, wherein the bone growth factor is chosen from the TGF β superfamily.

4. Resorbable bone substitute according to claim 3, wherein the
15 bone growth factor comprises TGF β .

5. Resorbable bone substitute according to claim 1, comprising 0,1-30 μ g bone growth factor per cm³ bone substitute material.

20 6. Resorbable bone substitute according to claim 1, comprising a carrier protein.

7. Resorbable bone substitute according to claim 6, wherein the carrier protein is chosen from blood serum proteins.

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8. Resorbable bone substitute according to claim 7, wherein the carrier protein comprises serum albumin.

9. Resorbable bone substitute according to claim 8, wherein the

carrier protein comprises human serum albumin.

10. Resorbable bone substitute according to claim 6, comprising per cm³ bone substitute material 0,1-4 mg carrier.

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11. Resorbable bone substitute according to claim 1, wherein the antimicrobial agent comprises an antimicrobial peptide being 10 to 25 amino acids in length, comprising a domain of at least 10 amino acids, consisting of two sterically oppositely arranged subdomains, 10 wherein the majority of the amino acids of the first subdomain being positively charged at physiological pH, and the majority of the amino acids of the second subdomain being uncharged at physiological pH.

12. Resorbable bone substitute according to claim 11, the 15 domain of the antimicrobial peptide being free of negatively charged amino acids at physiological pH.

13. Resorbable bone substitute according to claim 11, wherein the domain of the antimicrobial peptide being chosen from the 20 following sequences:

KRK FHEKHHS HRGY (Seq. ID No. 1)
KRLFKKLKFS LRKY (Seq. ID No. 2)
KRLFKLLFSLRKY (Seq. ID No. 3)
LLLFLKKRKKRKY (Seq. ID No. 4)
25 FKCRRWQWRMKKLG (Seq. ID No. 5)
GRRRRSVQWCA (Seq. ID No. 6)
SSSKEENRIIPGGI (Seq. ID No. 7),

the domain preferably being LLLFLKKRKKRKY (Seq. ID No. 4) or GRRRRSVQWCA (Seq. ID No. 6),

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14. Resorbable bone substitute according to claim 1, comprising curable bone cement material.

15. Resorbable bone substitute according to claim 1, comprising coated solid bone cement particles of biocompatible resorbable material, wherein the bone growth factor is incorporated in the particles, and the coat comprises the antimicrobial agent.

16. Resorbable bone substitute according to claim 1, comprising per g bone cement material:

0,1-10 µg growth factor,

0,1-10 mg antimicrobial peptide

17. Method for the preparation of a resorbable bone substitute according to claim 1, comprising the step of mixing a liquid aqueous component and a dry component comprising the bone cement powder material, wherein the preparation of the liquid component comprises the steps of:

- a) providing a first volume of a first aqueous medium, prepared by adding the bone growth factor in the said medium, comprising carrier protein,
- b) providing a second volume of a second aqueous medium.

18. Method according to claim 17, wherein the volume ratio between the first aqueous medium and the second aqueous medium is 1:1 - 1:10.

19. Method according to claim 17, wherein the bone growth factor comprises TGFβ.

20. Method according to claim 17, wherein the antimicrobial agent comprises an antimicrobial peptide being 10 to 25 amino acids in length, comprising a domain of at least 10 amino acids, consisting of two sterically oppositely arranged subdomains, wherein the majority of the amino acids of the first subdomain being positively charged at physiological pH, and the majority of the amino acids of the second subdomain being uncharged at physiological pH.

21. Kit for the preparation of a resorbable bone substitute according to claim 1, comprising:

- a liquid aqueous component comprising bone growth factor and carrier protein, and
- a solid component comprising powder bone cement material,

the antimicrobial agent being incorporated in the liquid or solid component or both, preferably in the solid component.

22. Kit according to claim 21, wherein the liquid component comprises, per g powder bone cement material:

- 0,2-20 µg bone growth factor, preferably TGFβ,
 - 0,2-8 mg carrier protein, preferably human serum albumin,
 - 0-20 mg antimicrobial agent, preferably an antimicrobial peptide as defined in claims 7-9, and
- 1 ml water or aqueous medium, wherein the amount of antimicrobial agent in the kit is at least 0,2 mg per g powder bone cement material.

23. Kit according to claim 21, wherein the aqueous component

comprises two aqueous subcomponents, the first subcomponent comprising the bone growth factor and the carrier in a first aqueous medium, the second subcomponent comprising a second aqueous medium, free of bone growth factor and carrier.

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